PATENT
Attorney Docket No. 06854.0024-01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Masahiro KAJIWARA	)	Group Art Unit: 1625
	)	
Application No.: 10/669,700	)	Examiner: D. Margaret M. Seaman
	)	
Filed: September 25, 2003	)	
	)	
For: UREASE INHIBITORS	)	Confirmation No.: 6367
	)	

Attention: Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY BRIEF UNDER 37 C.F.R. § 41.41

Pursuant to 37 C.F.R. §§ 41.41 and 41.39(b)(2), Appellant maintains the present appeal and presents this Reply to the Examiner's Answer (mailing date February 2, 2007) and the new ground of rejection contained therein. A Request for Oral Hearing is concurrently filed with this Reply Brief.

If any fees are required in connection with the filing of this paper that are not filed herewith, Appellant authorizes and requests that the required fees be charged to Deposit Account No. 06-0916.

I. Summary of Examiner's Answer

In her Answer, the Examiner continues to argue that Claim Group I (claims 9, 10, 12, 13, 15, 16, 18 and 20) and Claim Group II (claims 11, 17, and 19) are anticipated under 35 U.S.C. § 102(b) by Japanese Patent No. 04077476 to Hirai ("Hirai"). The prior rejection against claim Group III (claim 14) under § 102 was evidently dropped, but the claim group was newly rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Hirai in view of newly cited Richardson (Drugs, Sept. 1998, vol. 56(3), pp. 307-335) ("Richardson").

II. Response to Examiner's Answer

For the reasons set forth in Appellant's Appeal Brief and those herein, Appellant continues to disagree with the Examiner's rejections, including the new ground of rejection against claim Group III (claim 14).[1] Principally, the Examiner misapplies the legal standards for inherency by recognizing as a factual matter that not all ulcers are caused by urease or *H. pylori* but nevertheless contending that disclosure directed to treating ulcers necessarily entails treating ulcers caused by urease or *H. pylori*. Accordingly, reversal of the Examiner's rejections are respectfully requested.

A. Claim Group I: Claims 9, 10, 12, 13, 15, 16, 18, and 20

1. Summary Of Appellant's Position

Regarding this claim group, including the claimed "method of treating gastric mucosa injury caused by urease" (claim 9[2] (emphasis added)) and "method of treating gastroduodenal

[1] Pursuant to 37 C.F.R. § 41.39(b)(2), Appellant elects, in view of the Examiner's new ground of rejection against Claim Group III (claim 14), to maintain the present appeal and addresses the new ground of rejection in Section II.C, below.

[2] Claim 9. A method of treating gastric mucosa injury caused by urease, which comprises administering to a person in need thereof a therapeutically effective amount of an isothiazole compound represented by formula (1):

ulcer caused by Helicobacter pylori" (claim 20 (emphasis added)), the Examiner contends inherent anticipation, asserting that "Hirai teaches the treatment of ulcers which is the same patient population that is instantly being claimed because only a patient population having gastric mucosa injury would have an ulcer." (Answer, pg. 8.) In making this inherency argument the Examiner has wholly ignored the recitation that the claimed methods are directed to treatment of injury entailing a specified cause: urease or Helicobacter pylori ("*H.Pylori*").[3] Because the Examiner admits that it "is true" that not all ulcers are caused by urease or *H. Pylori* (Answer, pg. 10 (emphasis added)), treatment of ulcers according to Hirai is not inherently a treatment of ulcer caused by urease or *H. Pylori*.

Without citation to any evidence on the record, the Examiner contends that 9 out of 10 ulcers are caused by *H.Pylori*. (Answer, pg. 10.) Not only is this unreferenced statistic contrary to evidence of record, such as evidence cited in Appellant's Appeal Brief (*see, e.g.*, Section VII.A.3, and references cited therein), it is contrary to the Richardson reference relied upon by the Examiner in her new ground of rejection against claim 14 of the present application. For example, according to Richardson:

> NSAIDs are estimated to cause approximately 30% of ulcers. Their contribution to ulcer bleeding may even be greater than this, particularly if aspirin is taken into account. Prescribing of low dose aspirin is currently enhancing the number of bleeds associated with non-aspirin and aspirin NSAIDs. It can be calculated that

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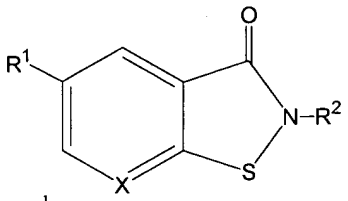

(1)

wherein R^1 represents a hydrogen atom or an amino group, R^2 represents a hydrogen atom, a lower alkyl group, or an acetyl group, and X represents a carbon atom or a nitrogen atom, or an adduct salt thereof.

[3] See specific recitations of claims 9, 10, 12, 13, 15, 16, 18 and 20.

> non-aspirin NSAIDs account for approximately 1200 deaths per annum in the UK in this way.

(Richardson, pg. 320 (citations omitted).) Richardson further states that:

> Next to *H. pylori,* NSAIDs are the most important cause of peptic ulceration, and may be even more important for ulcer complications such as perforations and bleeding.

(Richardson, pg. 328.)

Moreover, even if true that most ulcers might be caused by *H. pylori*, the evidence of record (*e.g.,* see above) plainly shows that some, indeed at least a very substantial fraction, of ulcers are not caused by urease or *H. pylori*. Therefore, treatment of ulcers according to Hirai is not inherently a treatment of injury or ulcer caused by urease or *H. Pylori*. Further, given that Hirai characterizes the activity of its compounds relative to the proton pump inhibitor ("PPI") activity of the PPI benchmark omeprazole, it is reasonable to conclude that one skilled would understand, if anything, that Hirai is directed to treatment of non-*H. pylori*, non-urease ulcers. Indeed, omeprazole is not indicated to be active against *H. pylori* or urease etiologies. (*See* Appeal Brief, Section VII.A.4, and references cited therein.)

The presently claimed methods are not inherent in Hirai's treatment of ulcers or other conditions at least because, in the large number of ulcer patients not having injury caused by urease or *Helicobacter pylori* infection, the use of a compound according to Hirai would not and cannot treat injury caused by urease or *Helicobacter pylori* when neither is present or where neither is the cause of injury. In this regard, the Richardson reference relied upon by the Examiner also makes it plain that therapies for *H. pylori* eradication and those for NSAID-caused ulcers are not interchangeable:

> Currently, there are no clear grounds for using *H. pylori* eradication as either an alternative or a supplement to omeprazole in NSAID users and for bleeding ulcers. Indeed, it has been

> recently shown in a Hong Kong study that omperazole is superior to *H. pylori* eradication for prevention of ulcer bleeding in non-aspirin NSAID users.

(Richardson, pg. 322 (citations omitted).)

As noted in Appellant's Appeal Brief (Brief at Section VII.A.2), the evidence of record relied upon to establish inherency "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference...." *Continental Can Co. USA, Inc. v. Monsanto Co.*, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) (emphasis added). Under these standards, and based on the evidence of record as well as the Examiner's admission (*e.g.*, Answer, pg. 10) that not all ulcers are caused by *H.Pylori*, the Examiner has not and cannot establish inherency of Claim Group I based on Hirai. This is the case, of course, even if treatment of injury caused by urease or *H.Pylori* "may result" from treatment of some patient according to Hirai. *Id.* ("Inherency... may not be established by probabilities or possibilities. Further, the mere fact that a certain thing may result from a given set of circumstances is not sufficient." (emphasis added)).

As explained in greater detail in Appellant's Appeal Brief (Brief at Section VII.A.2), *Perricone v. Medicis Pharmaceutical Corp.* is particularly relevant, in that it explains, *inter alia,* that the disclosed use of a compound for some broad application, *e.g.*, topical application to the skin, is not an inherent disclosure of using the compound to treat specific types of conditions or areas, *e.g.*, skin sunburn. 77 USPQ2d 1321, 1328 (Fed. Cir. 2005). Just as not all skin surfaces are skin sunburn surfaces, *Perricone* at 1328, not all ulcers are caused by urease or *H.Pylori*. Therefore, the treatment of ulcers is not an inherent disclosure of the treatment of gastric mucosa injury caused by urease or *H.Pylori*.

B. Claim Group 2: Claims 11, 17, and 19

Claims 11, 17, and 19 are directed towards treating chronic gastritis, as more specifically set forth therein. Although rejected as allegedly anticipated by Hirai, the rejection is deficient for all the reasons stated above with regard to Claim Group I. Further, the rejection is deficient in that the Examiner recognizes (at some points) a distinction between chronic gastritis and ulcer, but proceeds to ignore this distinction in arguing that treating ulcers according to Hirai inherently treats chronic gastritis.

Specifically, rather than identifying any disclosure in Hirai directed to method treating chronic gastritis (much less chronic gastritis caused by urease or *H.Pylori*), the Examiner contends that:

> (1) "[G]astritis is defines as inflammation of the stomach due action of a corrosive agent."
>
> (2) "The corrosive agent could be stomach acid...."
>
> (3) "...Hirai teaches the production of [stomach acid] will be suppressed by the use of the benzothiazole compounds."
>
> (4) "[Claim Group 2] use only the same compound as taught by Hirai, in the same patient population in the same manner as instantly claimed with the same outcome."

(Answer, pg. 11.) The Examiner concludes that the above "is inherency." (*Id.*) It is not.

In addition to the previous mentioned errors in the application of the inherency standards in the Answer, the Examiner equates ulcer treatment (regardless of origin or etiology) with, it seems, every conceivable gastric injury (regardless of source or etiology). In particular, while the Examiner relies on the definition of gastritis as "inflammation of the stomach due [to] action of a corrosive agent" (Answer, pg. 11), the Examiner separately states that an ulcer is "a hole in the stomach wall" (Answer, pg. 8). Missing, however, from the Examiner's Answer and position is any evidence for concluding that a reference directed to treatment of ulcers inherently

anticipates claims to methods of treating other, distinct injuries of specified etiologies, *e.g.*, a method of treating chronic gastritis caused by urease.[4] (See claim 11.) To the contrary, as noted above, the Examiner has properly recognized a distinction between gastritis and ulcers. In view of this recognition and the absence of any cited factual basis for the Examiner's position, the rejection contending that a method of treating ulcers is inherently a method of treating gastritis caused by urease or *H. pylori*, as more specifically set forth in the claims, necessarily fails.

C. Claim Group 3: Claim 14

Claim 14 was newly rejected in the Examiner's Answer under 35 U.S.C. § 103(a) as being allegedly unpatentable over Hirai in view of Richardson (Drugs, Sept. 1998, vol. 56(3), pp. 307-335) ("Richardson"). (Examiner's Answer, pg. 3.) This rejection is erroneous for at least the following reasons.

First, Richardson has not been cited for and does not overcome the aforemention deficiencies of Hirai with respect to claim 9, from which claim 14 depends. (See arguments addressing Claim Group I above and in Appellant's Appeal Brief, Section VII.A.)

Second, rather than cite any motivation for the proposed combination based on specific evidence of record, the Examiner relies upon *In re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA 1980) to argue that it would have been prima facie obvious to combine different types of pharmaceutically active agents. (Examiner's Answer, pg. 3-4.) However, the present case differs from the facts of *In re Kerkoven*. Moreover, it is impermissible for the Examiner attempt to rely on *Kerkhoven* as a short cut means to establishing a prima facie case of obviousness

[4] The Answer does include the continued (and mistaken) reliance on the Examiner's reported "same patient population" assertion (Answer at 11), but this assertion based on the population of ulcer patients has no bearing on the distinction of ucler treatment relative to chronic gastritis treatment.

without first establishing the elements of a prima facie case as required by the Supreme court in *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966).

Principally, the claims at issue in *Kerkoven* were directed to "A process for preparing a spray-dried detergent," 205 USPQ at 1070, and are therefore distinct from the "method of treating" as more specifically set forth in present claim 14. Furthermore, as characterized by the CCPA, the claims at issue in *Kerkoven* "require no more than the mixing together of two conventional spray-dried detergents." *Kerkoven* at 1072. The Examiner has not even suggested, much less pointed to any evidence, analogizing the combination of pharmaceutically active agents for a method of treating a person to mere mixing of conventional spray detergents. Indeed, the evidence appears to be to the contrary, with, for example, the Richardson reference indicating that *H. pylori* eradication therapy is distinct from and not interchangeable with the benchmark PPI, omeprazole. (Richardson, pg. 322 (quoted *supra*).)

III. Conclusion

For the reasons given above, pending claims 9-20 are allowable. Reversal of the Examiner's rejections are respectfully requested.

To the extent any extension of time is required to obtain entry of this Reply Brief, such extension is hereby respectfully requested. If there are any fees due that are not enclosed herewith, including any fees required for an extension of time, please charge such fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: April 2, 2007

By: _____
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